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Docket No. GJI-78
Serial No. 09/937,784Remarks

Claims 7-20 and 22 were pending in the subject application. By this Amendment, claims 7, 14, and 22 have been amended. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of the applicant's agreement with or acquiescence in the Examiner's position. Accordingly, claims 7-20 and 22 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicant and the applicant's representative wish to thank Examiner Sisson for the courtesy of the telephonic interview conducted with the undersigned on November 22, 2005, wherein it was agreed that the finality of the Office Action would be withdrawn. Although the Examiner did not agree that the rejections set forth herein under 35 U.S.C. §112, first paragraph, represent new grounds of rejection, the Examiner withdrew finality on the basis of the new obviousness-type double patenting rejection.

By this Amendment, the applicant has amended claims 7, 14, and 22 to recite that the target polynucleotide is isolated. Inherent support for this amendment can be found throughout the subject specification, such as the Example at pages 6-8, and particularly page 7, lines 11-24, which describes the formation of a target-primer complex from target and primer oligonucleotides, followed by injection of the primed DNA over the PcrA helicase on the sensor chip surface. Claims 7, 14, and 22 have also been amended to recite that the helicase and/or primase enzyme is immobilized. Support for this amendment can be found, for example, at page 5, lines 1-33; page 6, lines 32-34; page 7, lines 1-10, of the specification; and claims 13, 20, and 21 as originally filed. Claims 7, 14, and 22 have also been amended to recite the step of applying radiation to the reaction. Support for this amendment can be found, for example, at page 1, lines 28-33, of the specification. Claims 7, 14, and 22 have also been amended to recite that it is the applied radiation that is detected. Support for this amendment can be found, for example, at page 7, lines 31-34, and page 8, lines 1-5 and 12-15, and inherently throughout the specification.

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The specification has been objected to as improperly incorporating documents by reference. As an initial matter, pages 3-4 of the Office Action indicate that the specification includes the following "omnibus language":

[0065] Throughout this application, various publications, patents, and patent applications have been referred to. The teachings and disclosures of these publications, patents, and patent applications in their entireties are hereby incorporated by reference into this application to more fully describe the state of the art to which the present invention pertains.

The applicant cannot locate paragraph [0065] in the subject specification. The Examiner may be inadvertently referring to a different application. Clarification is respectfully requested. Moreover, there is no requirement that a patent application incorporate by reference nonessential subject matter contained in documents cited in the application. A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which the invention pertains to make and use the invention as of its filing date. *In re Glass*, 492 F.2d 1228, 181 USPQ 31 (CCPA 1974). Thus, the prior art setting may be mentioned in general terms. It is "the essential novelty, the essence of the invention, [that] must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention" MPEP 608.01(p). Accordingly, reconsideration and withdrawal of the objection to the specification is respectfully requested.

Claims 7-20 and 22 have been rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description. The specification provides an adequate written description of the claimed subject matter, conveying to one of ordinary skill in the art that the applicant was in possession of the claimed invention at the time the application was filed. The applicant has addressed each of the issues raised by the Examiner in the order they appear in the Office Action.

By this Amendment, the applicant has amended claims 7, 14, and 22 to address the issues raised by the Examiner in items 12-19 at pages 5-7 of the Office Action. To address item 12, as indicated above, the applicant has amended claims 7, 14, and 22 to recite the step of applying radiation to the reaction. Addressing item 13, as indicated above, the applicant has amended claims 7, 14, and 22 to recite that the target polynucleotide is isolated. To address item 14, as indicated above, the applicant has amended claims 7, 14, and 22 to recite that radiation is applied to the

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reaction, and it is the applied radiation that is detected. To address items 15 and 16, the applicant has amended claims 7, 14, and 22 to recite that the enzymes are immobilized. Furthermore, with respect to items 16-19, at pages 6-7, the Office Action indicates that the method encompasses the situation where unincorporated reactants are not removed from the reaction site. The Office Action appears to be referring to the unincorporated nucleotides in WO-A-99/0515. However, the reaction recited in the claims of the subject application does not involve incorporation of nucleotides. Reference to WO-A-99/0515 refers to the technique and apparatus used to detect the conformational change of the helicase. The present invention is based on the realization that monitoring a helicase enzyme as it unwinds a DNA helix allows the DNA to be sequenced. Furthermore, as indicated above, the amended claims recite that the enzyme is immobilized. Therefore, as indicated on page 5, lines 1-16, of the specification, the problem of noise from the interaction of a substrate that is not directly involved with the helicase, is reduced. Therefore, there is no requirement to remove these reactants from the reaction site. This is an advantage of the present invention.

With respect to item 20 at page 7, the applicant notes that the Office Action refers to a "polymerase enzyme." However, a "polymerase enzyme" is not recited in the claims. The applicant has amended claims 7, 14, and 22 in order to lend further clarity to the claimed subject matter. The subject specification provides relevant identifying characteristics sufficient to describe the claimed methods in such full, clear, concise, and exact terms that one of ordinary skill in the art would recognize that the applicant was in possession of the claimed invention. As the Examiner is aware, the Patent Office has the initial burden of presenting evidence or reasoning to explain why persons of ordinary skill in the art would not recognize in the original disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 263; 191 USPQ 90, 97 (CCPA 1976). The applicant submits that the Examiner has not introduced sufficient evidence or technical reasoning to shift the burden of going forward with contrary evidence to the applicant. Other than the issues enumerated as items 12-19 at pages 5-7 of the Office Action, which were presented for the first time in this Office Action, the Examiner does not articulate why the subject specification does not provide an adequate written description of the claimed subject matter.

In items 24-26, at pages 8-9 of the Office Action, it is stated that "no convincing evidence has been presented by the applicant's representative as to the level of skill, and to what one of ordinary

skill in the art would have been capable of doing.” To the contrary, the applicant has submitted numerous publications as evidence of the state of the art and, hence, the knowledge possessed by those of ordinary skill in the art. The applicant submitted copies of these publications with the supplemental Information Disclosure Statement that accompanied the applicant’s response dated March 28, 2005. The Examiner initialed each of the 18 citations listed on the PTO/SB/08, indicating that each reference was considered.

The applicant’s invention is based on a novel and non-obvious combination of well known materials and conventional techniques. The intricacies need not be detailed *ad absurdum*. The skill of the ordinary skilled person must be taken into account. *Merck & Co. v. Chase Chem. Co.*, 273 F.Supp. 68 (D.N.J. 1967). Further, where complexity dictates, broad terminology complies with the statute. *Application of Fuetterer*, 319 F.2d 259, 262 (1963); *Sears, Roebuck and Co. v. Jones*, 308 F.2d 705, 707, 708 (10th Cir. 1962).

The subject specification provides relevant identifying characteristics sufficient to describe the claimed invention in such full, clear, concise, and exact terms that one of ordinary skill in the art would recognize that the applicant was in possession of the claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, is respectfully requested.

Claims 7-20 and 22 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicant respectfully submits that the invention as currently claimed is reasonably enabled by the specification. The applicant has addressed each of the issues raised by the Examiner in the order they appear in the Office Action.

To the extent they are applicable to the instant rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the applicant’s foregoing remarks in response to the rejection for lack of written description are incorporated herein by reference in their entirety. To address item 28 at page 10 of the Office Action, the applicant has amended claims 7, 14, and 22 to recite the step of applying radiation to the reaction. Addressing item 29 at page 10 of the Office Action, the applicant has amended claims 7, 14, and 22 to recite that the target polynucleotide is isolated. To address item 30, the applicant has amended claims 7, 14, and 22 to recite that radiation is applied to the reaction, and it is the applied radiation that is detected. To address items 31 and 31, the applicant has

amended claims 7, 14, and 22 to recite that the enzymes are immobilized. Furthermore, the Office Action indicates that the method encompasses the situation where unincorporated reactants are not removed from the reaction site. The Office Action appears to be referring to the unincorporated nucleotides in WO-A-99/0515. However, as explained above, the reaction recited in the claims of the subject application does not involve incorporation of nucleotides. Reference to WO-A-99/0515 refers to the technique and apparatus used to detect the conformational change of the helicase. The present invention is based on the realization that monitoring a helicase enzyme as it unwinds a DNA helix allows the DNA to be sequenced. Furthermore, as indicated above, the amended claims recite that the enzyme is immobilized. Therefore, as indicated on page 5, lines 1-16, of the specification, the problem of noise from the interaction of a substrate that is not directly involved with the helicase, is reduced. Therefore, there is no requirement to remove these reactants from the reaction site. This is an advantage of the present invention.

The applicant respectfully submits that the meaning of the statement in item 33 at page 10 of the Office Action is unclear. For example, it is not clear if the Examiner is suggesting that the subject application does not enable sequencing of particular nucleic acids or certain lengths of polynucleotides. No reasonable basis for questioning the enablement of either aspect of the invention is presented, however.

In order to make a rejection based on non-enablement, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, F.2d 1557, 1562; 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). This the Examiner has not done. The Office Action does not articulate why, in view of the specification, one of ordinary skill in the art would lack information as to how to immobilize a helicase to a suitable solid support and how to carry out SPR analysis, for example. The mere fact that materials and methods cited in a patent application are not incorporated by reference does not shift the burden to the applicant to show that the patent application contains an enabling disclosure.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which the invention pertains to make and use the invention as of its filing date. *In re Glass*, 492 F.2d 1228, 181 USPQ 31 (CCPA 1974). As iterated in MPEP 608.01(p), the prior art setting may be mentioned in general terms. It is "the essential

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novelty, the essence of the invention, [that] must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention.”

The enablement requirement of 35 U.S.C. §112, first paragraph, does not require that the applicant reinvent the wheel. There is no need to inform the layman nor disclose what one of ordinary skill in the art already possesses.

Paragraph 1 permits resort to material outside of the specification in order to satisfy the enablement portion of the statute because it makes no sense to encumber the specification of a patent with all the knowledge of the past concerning how to make and use the claimed invention. One skilled in the art knows how to make and use a bolt, a wheel, a gear, a transistor, or a known chemical starting material. The specification would be of enormous and unnecessary length if one had to literally reinvent and describe the wheel. *Amtel Corporation v. Information Storage Devices, Inc.*, 198 F.3d 1374; 53 USPQ2d 1225 (Fed. Cir. 1999).

The Examiner is simply giving no credit (*i.e.*, according no knowledge) to those persons of ordinary skill in the pertinent arts of enzyme immobilization, surface plasmon resonance, or nuclear magnetic resonance, for example.

Given the teachings of the subject specification, and the knowledge of those skilled in the art, one of ordinary skill in the art would be able to make and use the invention without undue experimentation. The subject specification makes it clear that the method of the invention can be carried out by immobilizing helicase or primase enzymes on to a suitable substrate and monitoring the enzyme conformation by detecting changes in absorption of radiation that occur during the enzyme reaction. No undue experimentation would be required. Other than the issues enumerated as items 28-33 at page 10 of the Office Action, which were presented for the first time in this Office Action, the Examiner does not specify what aspects of the method of the invention would require undue experimentation and **why**.

The applicant respectfully submits that the subject specification enables one of ordinary skill in the art how to make and use the invention without resort to undue experimentation. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, is respectfully requested.

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Claims 7, 8, 11, 13-16, 18, 20, and 22 have been rejected under the judicially created doctrine of "obviousness-type" double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,623,929 (hereinafter referred to as the '929 patent). The applicant respectfully submits that the claims of the subject application are not obvious over the indicated claims of the cited patent. The Office Action indicates that claims 1-5 of the '929 patent are drawn to a method of sequencing a nucleic acid. This is incorrect. Claims 1-5 of the '929 patent are in fact drawn to a method for polynucleotide synthesis. Measuring a change in, or absorption of, radiation to determine the sequence of a target polynucleotide is not suggested. There is nothing in the claims of the '929 patent that suggest the method for polynucleotide synthesis of the subject invention as currently claimed. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.


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The applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Petition and Fee for Extension of Time

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